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NONSUICIDAL SELF-INJURY AND EMOTION REGULATION – CLINICAL CORRELATES AND NOVEL TREATMENTS

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Nonsuicidal Self-Injury and Emotion Regulation – Clinical Correlates and Novel Treatments

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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Don't forget to go home.

ABSTRACT

Background: Nonsuicidal self-injury (NSSI) and NSSI disorder are common, particularly among adolescents and young adults, and have been associated with several adverse outcomes, including general psychopathology and suicide. It has been recommended to study self-injury separately from suicidal behaviors to better understand its etiology and maintaining factors. One factor that may be important to understanding NSSI is emotion regulation. The Difficulties in Emotion Regulation Scale (DERS) is a useful measure of the construct; however, for a measure to have broad research and clinical utility it must be brief. Despite the clinical relevance of NSSI, treatments that specifically target the behavior are scarce. One exception is emotion regulation group therapy (ERGT) that was developed to directly target NSSI and its proposed underlying mechanism of difficulties in emotion regulation. Although ERGT has shown promise in reducing adult NSSI and related difficulties it has never been evaluated under “real-world” conditions delivered by community clinicians, nor has it been tested in adolescents. Despite the clinical relevance, many individuals with NSSI never get access to empirically supported treatments. There is evidence, that online interventions could increase the availability of effective treatments but online therapy has never been evaluated for NSSI.

Aims: The aim of the present thesis was to study clinical and psychosocial correlates and outcomes associated with NSSI, to develop a brief measure of emotion regulation, and to develop and evaluate novel treatments that can be easily and widely implemented for individuals who engage in NSSI.

Methods: In Study I, we conducted a case-control study (N = 25,161) and a longitudinal cohort study (N = 5,370) using data from a regional clinical care register and Swedish national registers. We compared clinical and psychosocial correlates and subsequent adverse outcomes in three groups of adolescent patients who presented to child and adolescent mental health services with self-injury only, self-injury with suicidal ideation and behaviors, and patients without any indication of self-injury or suicidal ideation and behavior. In Study II, we developed a 16-item version of the DERS (DERS-16) and investigated its reliability and validity in a clinical sample (N = 96) and two community samples (Ns = 102 and 482). In Study III, we studied ERGT in a multi-site uncontrolled trial (N = 95). In Study IV, we adapted ERGT for adolescents to a novel emotion regulation individual therapy (ERITA) protocol that we evaluated in 17 adolescents with NSSI disorder and their parents, using an uncontrolled trial design. Finally, in Study V, we developed an online version of ERITA and included 25 adolescents with NSSI disorder and their parents in an uncontrolled pilot trial. In all intervention studies, measures were administered pre-treatment, post-treatment and at 6-month follow-up. Mediation analyses were conducted in Studies IV and V.

Results: In Study I, results demonstrated that adolescent patients with self-injury with and without suicidal ideation and behavior were more burdened in terms of clinical care utilization, global functioning, mental disorders, and psychosocial problems than the clinical controls, and were at greater risk for several important adverse outcomes in emerging adulthood. Although the self-injury group was more burdened and at greater risk compared to controls, they were not as burdened as the self-injury with suicidal ideation and behavior group. Results from Study II showed that the shortened DERS-16 demonstrated excellent internal consistency, good test-retest reliability, and good convergent and discriminant validity. In all treatment studies (Studies III-V), treatment compliance and measures of credibility were acceptable, and participation in treatment was associated with significant reductions in NSSI and related difficulties. Moreover, change in difficulties in emotion regulation mediated week-to-week changes in NSSI frequency in Studies IV and V.

Conclusions: Self-injury with and without suicidal ideation and behaviors should inform risk assessment and be prioritized within child and adolescent mental health services. The DERS-16 is a valid and brief self-report measure of difficulties in emotion regulation. It is feasible to implement ERGT within a community-based health care system. ERITA may be a promising treatment for NSSI among adolescents, both in a traditional face-to-face format, and in an online format. Due to treatment length and format, ERGT and ERITA carry the potential to increase access to psychological treatments for adults and youth with NSSI. Also, in line with the theoretical model underlying the ERITA interventions, improvement in difficulties in emotion regulation mediates reduction in NSSI during treatment, thus providing further preliminary support for the underlying role of emotion regulation difficulties in the maintenance of self-destructive behaviors.

LIST OF SCIENTIFIC PAPERS

- I. Bjureberg, J., Ohlss, A., Ljótsson, B., D'Onofrio, B. M., Hedman-Lagerlöf, E., Jokinen, J., Sahlin, H., Lichtenstein, P., Cederlöf, M., Hellner, C. Adolescent Self-Harm With and Without Suicidal Ideation and Behaviors: Cross-sectional and Longitudinal Analyses of a Swedish Regional Register. Submitted.
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LIST OF ABBREVIATIONS

BIP	<i>Barninternetprojektet</i> (Child Internet Project)
BPD	Borderline personality disorder
BPFSC	Borderline Personality Feature Scale for Children
CAMHS	Child and Adolescent Mental Health Services
CBT	Cognitive behavioral therapy
CGAS	Children's Global Assessment Scale
CI	Confidence interval
CFA	Confirmatory factor analysis
DBT	Dialectical behavioral therapy
DERS	Difficulties in Emotion Regulation Scale
DERS-16	Difficulties in Emotion Regulation Scale, 16-item version
DSH	Deliberate self-harm
DSHI	Deliberate Self-Harm Inventory
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
ERGT	Emotion regulation group therapy
ERITA	Emotion regulation individual therapy
EAM	Experiential avoidance model
fMRI	Functional magnetic resonance imaging
HPA axis	Hypothalamic-pituitary adrenocortical axis
HR	Hazard ratio
ICBT	Internet-delivered cognitive behavioral therapy
MBT	Mentalization-based treatment
NSSI	Nonsuicidal self-injury
OR	Odds ratio
RCT	Randomized controlled trial
SD	Standard deviation
SH	Self-harm
SIB	Suicidal ideation and behaviors

1 INTRODUCTION

Nonsuicidal self-injury (NSSI) is highly prevalent and associated with suffering for the individual and the afflicted family. Despite the clinical relevance of this behavior, there remains a continued need to examine factors that maintain NSSI, the relation between NSSI and suicidal behavior, and outcomes associated with NSSI. Further, treatments developed specifically to target NSSI are scarce and most that are available have limited empirical support.

My interest in NSSI and emotion regulation grew during my first years as a clinical psychologist at a unit specializing in dialectical behavioral therapy and borderline personality disorder (The Borderline Unit, Psychiatry Northwest) in Stockholm, Sweden. Individuals with NSSI are often misunderstood within healthcare and there are few treatment options available for this population. After lengthy discussions with my experienced and supporting mentors and colleagues, we decided to develop an early intervention for self-injurious behavior that carried the potential to improve psychological well-being and prevent further deterioration in mental health. This ambition timed well with the newly developed government-funded National Self-Injury Project¹. Many hard-working clinicians, peer supporters, and researchers in this project have made these studies possible.

This thesis describes the process of how I, together with colleagues, national and international collaborators, and supervisors, learned about the course of NSSI, its underlying processes, and developed and evaluated treatments that can be easily and widely implemented. The results presented are limited by design and method. However, they do point us in certain directions and given that this research endeavor has only just begun, I hope that it will serve as the foundation for a larger body of future research in this area.

Stockholm, February 2018.

¹ A national developmental project initiated by the Swedish Ministry of Health and Social Affairs (*Socialdepartementet*) in collaboration with the Swedish Association of Local Authorities and Regions (*Sveriges Kommuner och Landsting*). Please visit <https://nationellasjalvskadeprojektet.se/english/> for more information.

2 BACKGROUND

2.1 NONSUICIDAL SELF-INJURY AND NONSUICIDAL SELF-INJURY DISORDER

2.1.1 DEFINITION AND CLASSIFICATION

Nonsuicidal self-injury (NSSI; also referred to as deliberate self-harm; DSH) has been defined as “the deliberate self-inflicted destruction of body tissue without suicidal intent and for purposes not socially sanctioned” [1]. Self-injury is most often inflicted with a knife, needle or razor and common areas for injury include the arms, legs and abdomen [2-4]. Within the definition of NSSI lies several important delimitations, touching on the current debate on how to best define self-injurious behaviors [5-8]. First, this definition does not include indirect and accidental self-injurious behaviors, such as disordered eating and drug abuse. Second, NSSI refers to the destruction of body tissue, omitting nonsuicidal self-poisoning (a behavior included in other definitions of self-injury [9]). Finally, the term only includes self-injurious behaviors that were engaged in without suicidal intent. Concern has been raised that the distinction between non-suicidal and suicidal behaviors is difficult to make in a reliable manner. For example, opponents argue that underlying motivations may be unclear even to the individual engaging in the behavior, and, because the distinction is based on the individual’s own recollection, this may introduce biased and inaccurate statements [8]. However, there is evidence demonstrating that NSSI most often occurs without suicidal thoughts [10], suggesting that NSSI may be studied separate from suicide attempts. Although the term NSSI is debated [6,8], both clinicians and researchers have likely benefited from the increased clarity in terms and classifications that has emerged within the field the last few years [11].

Prior research has to a great extent focused on NSSI in the context of borderline personality disorder (BPD), as self-injury is one of nine diagnostic criteria of BPD [12]. However many individuals who engage in NSSI do not fulfill criteria for this disorder [13-15]. NSSI has gained increased scientific attention by itself, and was recently included on its own as a tentative diagnostic entity within Section 3 (“conditions for further study”) in the fifth edition of the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-5 [12]). The main criteria for the proposed NSSI disorder include that NSSI has occurred on five or more days within the last year. Furthermore, the individual engages in the behavior with the expectation of either obtaining emotional or cognitive relief, to resolve an interpersonal difficulty, and/or creating a positive feeling state [12]. See Table 1 for the proposed DSM-5 criteria for NSSI disorder.

Table 1. Proposed criteria for Nonsuicidal Self-Injury Disorder Criteria in DSM-5

-
- A. In the last year, the individual has, on 5 or more days, engaged in intentional self-inflicted damage to the surface of his or her body of a sort likely to induce bleeding, bruising, or pain (e.g., cutting, burning, stabbing, hitting, excessive rubbing), with the expectation that the injury will lead to only minor or moderate physical harm (i.e., there is no suicidal intent). Note: The absence of suicidal intent has either been stated by the individual or can be inferred by the individual's repeated engagement in a behavior that the individual knows, or has learned, is not likely to result in death.
- B. The individual engages in the self-injurious behavior with one or more of the following expectations:
1. To obtain relief from a negative feeling or cognitive state.
 2. To resolve an interpersonal difficulty.
 3. To induce a positive feeling state.
- Note:** The desired relief or response is experienced during or shortly after the selfinjury, and the individual may display patterns of behavior suggesting a dependence on repeatedly engaging in it.
- C. The intentional self-injury is associated with at least one of the following:
1. Interpersonal difficulties or negative feelings or thoughts, such as depression, anxiety, tension, anger, generalized distress, or self-criticism, occurring in the period immediately prior to the self-injurious act.
 2. Prior to engaging in the act, a period of preoccupation with the intended behavior that is difficult to control.
 3. Thinking about self-injury that occurs frequently, even when it is not acted upon.
- D. The behavior is not socially sanctioned (e.g., body piercing, tattooing, part of a religious or cultural ritual) and is not restricted to picking a scab or nail biting.
- E. The behavior or its consequences cause clinically significant distress or interference in interpersonal, academic, or other important areas of functioning.
- F. The behavior does not occur exclusively during psychotic episodes, delirium, substance intoxication, or substance withdrawal. In individuals with a neurodevelopmental disorder, the behavior is not part of a pattern of repetitive stereotypies. The behavior is not better explained by another mental disorder or medical condition (e.g., psychotic disorder, autism spectrum disorder, intellectual disability, Lesch-Nyhan syndrome, stereotypic movement disorder with self-injury, trichotillomania [hair-pulling disorder], excoriation [skin-picking] disorder).
-

Note. Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorder, Fifth edition, (Copyright © 2013). American Psychiatric Association.

Given that the criteria for NSSI disorder were only recently established, most empirical studies in the field of NSSI, with some exceptions, have studied NSSI-behavior (later referred to as NSSI), not the NSSI diagnosis (later referred to as NSSI disorder). This is reflected in the research review below.

2.1.2 PREVALENCE

The average age of NSSI onset is between 13-14 years [16-18], and the behavior is common in both community and clinical samples. The pooled lifetime international prevalence of NSSI in nonclinical samples is approximately 17% among adolescents, 13% among young adults,

and 6% among adults [19]. NSSI is even more prevalent in clinical samples ranging from 40 to 82% among adolescents [2,3,20,21] and 19-25% among adults [22]. The prevalence of NSSI disorder has been estimated to range from 1.5 to 6.7% [18,23-25] in child and adolescent community samples, and 0.3% in an adult community sample [26].

A common misconception is that NSSI almost exclusively occurs among women. Although most research has shown that NSSI is about twice as common among adolescent females than adolescent males [27,28], some studies show no sex differences in prevalence for adolescents and young adults [19,29,30]. One meta-analysis on gender differences in the prevalence of NSSI concluded that NSSI is significantly more common among women than men but the difference was small (odds ratio [OR] = 1.5). They also found that gender differences in prevalence were larger for clinical samples, compared to community samples. Finally, although self-cutting was more common among females than males, no statistically significant difference was found in this study for any other method (e.g., punching [31]).

2.1.3 CORRELATES, RISK FACTORS AND ETIOLOGY

2.1.3.1 Diagnostic correlates

A large majority of individuals that engage in NSSI fulfill diagnostic criteria for one or several psychiatric disorders [13,14,32]. Nock et al. [14] found that that 87.6% of a sample of in-patient adolescents with NSSI met DSM-IV diagnostic criteria for at least one Axis I disorder, where depression, conduct disorder, and PTSD were among the most common. In this study, half of the sample met criteria for BPD.

Psychiatric comorbidity has also been investigated in adolescents fulfilling diagnostic criteria for NSSI disorder [13,32]. For example, Glenn et al. [13] found that 73.5% also had a diagnosis of depression, 66.3% had an anxiety disorder and 51.7% had BPD.

2.1.3.2 Risk factors for NSSI

Studies of correlates and risk factors are important to better understand the etiology, predict, and ultimately prevent and treat a condition. The majority of studies on NSSI are cross-sectional; however, to specify the exact nature of the association, longitudinal studies capturing the temporal relationship between the risk factor and outcome of interest, are much-needed. One of the most comprehensive meta-analysis on risk factors for NSSI including prospective longitudinal studies [33], concluded that few strong risk factors for the behavior have been identified. The strongest risk factors (ORs > 3.0) included cluster B personality disorders, prior history of NSSI, and hopelessness. Less strong risk factors (ORs near 2.0) were former suicidal thoughts/behaviors, self-reported likelihood of engaging in NSSI in the future, exposure to peer NSSI, and abuse. Several factors that have demonstrated strong associations in cross-sectional research such as emotion dysregulation and symptoms of depression and anxiety (e.g., [34,35]) were not meaningful predictors of NSSI in this study

[33]. However, in this meta-analysis the authors [33] speculate that even though these factors are not strong risk factors on their own, they could still contribute to the maintenance of NSSI engagement. Moreover, findings from this meta-analysis should be interpreted with caution because the strength of the associations found in the included studies in this review varied significantly depending on NSSI assessment method (measurement type and if NSSI was measured on a binary versus continuous scale), sample type, and age. Thus, after adjusting for publication bias in this study, the overall mean OR was rather low. Finally, these findings should be reviewed knowing that the included studies in the meta-analysis had a median follow-up period of 12 months; hence, it is possible that potential risk factors not identified in this study can constitute stronger risk for NSSI when studied over shorter periods of time. Finally, critics claim that producing a single list of the most important risk factors is a “one-dimensional” approach that limits our understanding. It may be more meaningful to consider several factors together [36]. With this in mind, some of the most commonly studied correlates and risk factors potentially part of the etiology of the behavior are described below.

Childhood experiences. One well-studied correlate of self-injury is childhood maltreatment, especially childhood sexual abuse [37]. Indeed, a recent meta-analysis found that overall childhood maltreatment was associated with NSSI with a medium effect size (OR = 3.42) and the specific association with childhood sexual abuse was OR = 2.65 [38]. Being bullied by peers in childhood [39] and having dysfunctional relationships [40] are other examples of psychological burden in adolescence that may constitute risk factors for NSSI. One review has proposed that social contagion (i.e., influence from friends or idols) may increase the likelihood that an individual engages in NSSI for the first time, however the continuation of NSSI is probably related to other factors [41]. There are also studies establishing a clear link between identification with certain youth subcultures and NSSI [42,43], with one recent meta-analysis demonstrating that identifying with the *emo* subculture is associated with increased risk of engaging in NSSI [43].

Sexual orientation. In a systematic review among adolescents, Batejan et al. [44] demonstrated that non-heterosexual orientation (bisexual orientation in particular) is associated with NSSI with a medium-to-large effect size. The well-cited minority stress theory [45], proposes that the experience of stress (e.g., prejudice and discrimination) among sexual minorities may lead to adverse mental health effects and risk behaviors such as NSSI.

2.1.3.3 Neurobiological correlates

Most studies on neurobiological factors related to NSSI have been conducted in the context of adults with BPD (e.g., [46-48]); however, there are some efforts focused on studying this behavior independent of diagnosis (for a review, see Schreiner et al. [49]). As will be described in further detail later, the most common self-reported purpose of NSSI is to regulate negative emotions [50]. Negative affect has repeatedly been shown to be associated with cortico-limbic neurocircuitry [51]. Thus, this is one of the brain areas that has accumulated most of the

research interest in the study of circuits and physiology involved in NSSI. Below, a brief summary of the research field will be presented. In this section, recent research on the gene x environment interaction prediction of NSSI, will also be discussed. However, it is important to note that the field of neurobiology in NSSI is still in an early stage, thus the findings from single cross-sectional studies should be interpreted with caution. Further, without longitudinal research delineating the temporal nature, it is impossible to know if the biological findings are part of the cause of NSSI or if they are important correlates to behavioral processes such as classical and operant conditioning theorized to be involved in the maintenance of NSSI (described later in this thesis).

Circuits. One study using functional magnetic resonance imaging (fMRI) found differentiations in the limbic system when comparing adolescents with NSSI to adolescents without NSSI when they processed emotional stimuli, indicating deficits in emotion regulation in the brain of adolescents with self-injury [52]. In line with theory and research on interpersonal stressful events and NSSI [3], another study using fMRI has shown differentiated processing of social exclusion in the medial prefrontal cortex and the ventrolateral prefrontal cortex, indicating that youth with NSSI may be more affected by social exclusion compared to those without [53].

Because pain is inherent to NSSI, the potential rewarding effects of pain perception have been studied in this context. Indeed, differences during pain offset (i.e., the removal of pain) has been found using both self-report data as well as neuroimaging data for individuals with NSSI [54]. Specifically, it has been found that although adolescents and young adults with and without NSSI display similar levels of pain in response to pain stimuli, the NSSI group report greater levels of pain relief after withdrawal from the pain stimuli. This relief was correlated with blood oxygen level dependent signal within the dorsal striatum, an area that has been tied to reward circuitry [54]. Research on relief from pain has shown that the removal of physical pain simultaneously simulates positive affect and diminishes negative affect, which may be part of the reinforcing consequences of NSSI. Indeed, the cerebrospinal fluid levels of endogenous opioids, that are related to pain perception, has been shown to be different in individuals with NSSI compared to clinical controls. Specifically, B-endorphin and met-enkephalin levels were significantly lower for the NSSI group, providing evidence for the involvement of endogenous opioid system in NSSI [55]. However, in lack of longitudinal studies any conclusions regarding causality are precluded.

Physiology. As many individuals with NSSI report that they engage in the behavior in response to stress [56], several studies have focused on the hypothalamic-pituitary adrenocortical (HPA) axis. This is an area known to be involved in the coping of stressful situations [57-59]. Further, early life adversity, prevalent in individuals with NSSI, is associated with HPA axis dysregulation possibly via epigenetic mechanisms (for a review see [60]). Indeed, individuals with NSSI have been shown to have a heightened cortisol awakening response [57], an efficient negative feedback loop [58], and hyporesponsiveness of

the HPA axis in acutely stressful situations [59]. Further, worth noting is that HPA axis dysregulation has also been reported in several studies of suicide attempters and suicide victims [61].

Genes. There is limited research in this area; however, an interaction between gene and environment in relation to NSSI has been found. One study indicated that short carriers of the Serotonin Transporter-linked Polymorphic Region (5-HTTLPR) who experienced chronic interpersonal stress had the highest level of NSSI engagement [62].

2.1.4 COURSE AND SUBSEQUENT OUTCOMES

In a recent systematic review of the course of NSSI (also including some studies with self-injury with unclear suicidal intent), Plener et al. [63] found that in longitudinal studies among adolescents, the trend was that rates of NSSI increased over time. However, in studies of older adolescents and young adults, there was a trend for rates to decrease during follow-up. The authors concluded that peak prevalence of NSSI is found during adolescence at around 15 to 17 years of age and that remission is expected for most in young to middle adulthood. However, it is important to note that although many individuals cease the behavior within a few years, it does have a more chronic course for some [4]. Further, Plener et al. [63] raised the concern that even if individuals cease with repetitive NSSI they may still be at risk of using other maladaptive emotion regulation strategies. Indeed, one recent study has demonstrated that teenagers with previous NSSI are more likely to show high levels of substance misuse [64].

Little is known about the subsequent outcomes associated with NSSI, as most studies have not differentiated between nonsuicidal and suicidal self-injury. However, in one of the few exceptions, Mars et al. [65] demonstrated that adolescents with NSSI had elevated risks of developing a range of mental problems (including depression and anxiety disorders) at age 16 years, recurrent episode of self-injury, and problem substance misuse, emphasizing the need for early identification and treatment of youth who engage in NSSI. Few long-term follow-up studies exist (and to my knowledge none on NSSI). However, one recent study followed adolescents with self-injurious behaviors for approximately 15 years and found a wide range of psychosocial problems at follow-up, including mental health problems, illicit drug use, and unemployment. Yet, it is important to note that most associations attenuated after controlling for adolescent mental disorders [66]. I am not aware of any longitudinal studies that have studied the course of NSSI disorder.

2.1.4.1 Suicide

As previously discussed, the relation between self-injury without suicidal intent and actual suicide attempts is a complex issue. Even though NSSI per definition is performed without suicidal intent and seldom co-occurs with suicidal thoughts [10], several studies indicate that NSSI is a risk factor for later suicide attempt and completed suicide. Longitudinal findings

have shown that NSSI predicts suicide attempts even after controlling for a history of suicidal behavior [67-69]. These findings indicate that early effective interventions for those who engage in NSSI could potentially have a suicide preventive effect.

2.1.5 THEORETICAL MODELS OF NSSI

NSSI was once regarded as an unusual marginal component of psychiatric populations or developmentally disabled cohorts, but it may be better understood as a relatively common way for individuals to manage emotional pain and to cope with interpersonal difficulties [70]. NSSI can serve a multitude of functions for individuals engaging in these behaviors. As reflected in the DSM-5 criteria for NSSI disorder [12], the different functions of NSSI can be divided into two categories: intrapersonal (i.e., relief from aversive affective and/or cognitive state) and interpersonal (e.g., relief from social demands). The most commonly reported functions of NSSI are intrapersonal [50]. This intrapersonal function is largely driven by difficulties in emotion regulation [71,72].

The two most cited theoretical models specifically developed for NSSI is Chapman et al's [71] experiential avoidance model (EAM) of NSSI and Nock's [73] integrated theoretical model of the development and maintenance of NSSI. Both models use a functional perspective to describe the maintenance of NSSI.

2.1.5.1 The experiential avoidance model of NSSI

Chapman et al. [71] have proposed the EAM model of NSSI, which is based on behavioral theory. This model emphasizes difficulties in emotion regulation, and poses that NSSI is primarily maintained through negative reinforcement in the form of avoidance of aversive emotional experiences. In contrast to previous models of self-injury, which have focused more specifically on certain populations (e.g., individuals with BPD [72]), the EAM was developed to describe the maintenance of NSSI across different populations. As illustrated in Figure 1, the EAM proposes that NSSI is maintained by escape conditioning and negative reinforcement. The model describes how a stimulus triggers an unwanted emotional response, and the individual experiences an urge to avoid this experience. Due to low availability of more adaptive responses, the individual engages in NSSI, which reduces the emotional arousal, thus negatively reinforcing the behavior. Through repetition of negative reinforcement, the association between unwanted emotional arousal and NSSI is strengthened, and as a result, NSSI becomes an automatic escape response. Chapman et al. [71] argue that although NSSI likely has several determinants, the role of experiential avoidance in NSSI is well-established in the literature and is helpful to understand the maintenance of the behavior.

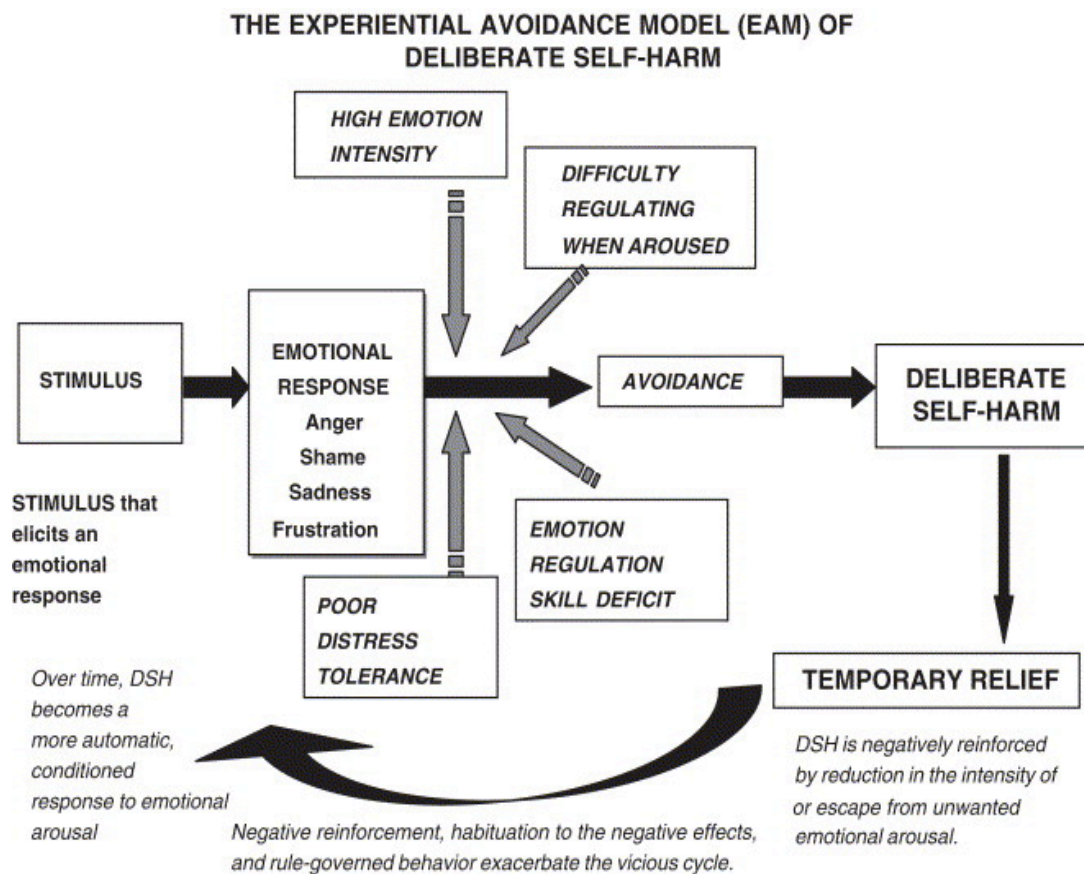


Figure 1. Graphic depiction of the Experiential Avoidance Model (EAM) of deliberate self-harm (DSH). In: Chapman, A. L., Gratz, K. L., & Brown, M. Z. (2006). Solving the puzzle of deliberate self-harm: The experiential avoidance model. *Behaviour Research and Therapy*, 44, 371-394. Reprinted with permission from Elsevier.

2.1.5.2 The integrated theoretical model of the development and maintenance of NSSI

Nock [73] adopts an integrated perspective, including findings from different areas of research. According to his model, distal risk factors (such as genetic predisposition for emotional/cognitive reactivity and childhood abuse) make the individual vulnerable through deficits in distress tolerance and interpersonal skills, which in interaction with NSSI-specific vulnerability factors (e.g., social learning, self-punishment) lead the individual to engage in NSSI in response to stressful events instead of using more adaptive strategies. NSSI is then maintained because of its short-term effectiveness in regulating aversive emotional experiences and social situations [73].

2.1.6 STIGMA

Growing awareness of the high prevalence of NSSI among adolescents has provided school and health care services with new challenges. NSSI causes great concern among staff in various settings [74] and individuals who engage in NSSI often report negative responses from professionals [75]. Although NSSI is a serious condition, many individuals who engage

in self-injury never seek help [76-78] or tell others about the behavior [79]. The stigma and shame associated with NSSI [80] is probably an important barrier to treatment-seeking [81].

2.2 EMOTION REGULATION

2.2.1 DEFINITION

Interest and empirical research on emotion regulation has increased rapidly over the past two decades [82]. According to Thompson [83, pp. 27-28], emotion regulation refers to “extrinsic and intrinsic processes responsible for monitoring, evaluating, and modifying emotional reactions, especially their intensive and temporal features, to accomplish one's goals”.

However, emotion regulation has been defined in several ways, with some conceptualizations emphasizing the ability to control emotional experience, expression, and reduction of emotional arousal [84,85]. In contrast, other conceptualizations of emotion regulation emphasize that all emotions are functional [86-88]. Inherent in these latter conceptualizations of emotion regulation, is the concept that emotions are functional because they provide information about ourselves, our environment, and motivate behaviors that may facilitate situationally appropriate behaviors [89]. This implies that difficulties in the awareness, understanding, or modulation of emotions may interfere with adaptation to situational demands and contribute to various unwanted outcomes. A steady increasing body of research offers empirical support for emotion regulation deficits as an underlying mechanism in a wide range of psychopathology and risky behaviors (for a review, see Sheppes et al. [90]), including NSSI [34].

2.2.2 ASSESSMENT OF EMOTION REGULATION

Given the obvious clinical relevance of emotion regulation, several questionnaires have been developed, designed to measure different aspects of the construct (e.g., [91-95]). One of the most well-established measures of emotion regulation is the Difficulties in Emotion Regulation Scale (DERS [96]). The DERS is a 36-item self-report measure that assesses different aspects of difficulties in emotion regulation. The DERS was developed to be a clinically useful instrument based on the latter conceptualization described above.

Specifically, the DERS aims to measure the: “(a) awareness, understanding, and acceptance of emotions; (b) ability to engage in goal-directed behaviors and inhibit impulsive behaviors when experiencing negative emotions; (c) flexible use of situationally-appropriate strategies to modulate the intensity and/or duration of emotional responses, rather than to eliminate emotions entirely; and (d) willingness to experience negative emotions as part of pursuing meaningful activities in life” [87, p. 1094].

2.3 TREATMENTS SPECIFIC TO NSSI

To date, treatments specifically designed to target NSSI are scarce [97-100]. Turner et al. [100] concluded that no treatment for NSSI, neither for adults nor adolescents, qualifies as

empirically supported according to well-established criteria [101]. However, there are some treatments that hold promise in the treatment of NSSI.

2.3.1 PHARMACOLOGICAL TREATMENT FOR NSSI

Among psychopharmacological treatments for NSSI, five drug classes have been studied: SSRI, atypical antipsychotics, SNRI, opioids, and opioid antagonists [100]. A recent Cochrane review on pharmacological treatments for self-injury in adults conclude that the low quality and small number of conducted trials precludes any conclusions regarding the efficacy of any pharmacological intervention [102]. Another Cochrane review on treatments for self-injury in children and adolescents from the same year and research group could not identify one single trial on pharmacological treatments that met the set criteria to be included in the meta-analysis [98]. Thus, clinical guidelines state that psychopharmacological treatments should not be prescribed as a specific intervention to reduce self-injury [11,103].

2.3.2 PSYCHOLOGICAL TREATMENT FOR NSSI

Randomized controlled trials (RCTs) of psychological treatment effectiveness for NSSI are few and the results are inconclusive [100]. Concern has been raised that only a small number of therapeutic treatments have been developed and evaluated specifically for NSSI. Most studies that have been conducted in the field have included individuals that engage in self-injury both with and without suicide intent [104]. Failing to distinguish lethal intent and the usage of vague and inconsistent terms and definitions makes it difficult to understand what mechanisms and behaviors that the different treatments address. One of the most recent and thorough meta-analysis on psychotherapeutic treatment for self-injury [99] identified dialectical behavioral therapy for adolescents (DBT-A [105]) and mentalization-based treatment for adolescents (MBT-A [106]) to be potentially effective for NSSI². However, when analyzing NSSI separately from suicide attempts, neither DBT-A nor MBT-A were superior to treatment as usual [99]. In another systematic review of interventions for NSSI in both adolescent and adult populations, Turner and colleagues [100] concluded that among the interventions that may be effective in reducing NSSI frequency are dialectical behavior therapy (DBT [72]), emotion regulation group therapy (ERGT [107]), manual-assisted cognitive therapy [108], and dynamic deconstructive psychotherapy [109]. DBT is the treatment that has been most extensively researched and is often the treatment of choice. However, results regarding the efficacy of DBT for NSSI are mixed. At least three RCT:s have shown that DBT leads to greater reductions in NSSI frequency when compared to TAU [105,110,111], whereas two other RCTs demonstrated that reductions in NSSI frequency were not statistically significant when DBT was compared to active control conditions [112,113]. Furthermore, the most popular treatments for NSSI (i.e., DBT and MBT) do not

² Cognitive behavioral therapy (CBT) was also identified as a promising treatment in this meta-analysis; however, the study that examined CBT only included suicide attempts as an outcome, not NSSI.

only aim at reducing NSSI-frequency, but also other symptoms of BPD, and the treatments are comprehensive, time-consuming, and costly (one to two years of treatment including both weekly individual therapy sessions and skills training in group). Therefore, less intensive, shorter, focused and less expensive psychological interventions have been called for by researchers and clinicians [114].

2.3.3 EMOTION REGULATION GROUP THERAPY (ERGT)

ERGT [107] is an acceptance-based behavioral therapy that was designed to address the need for an effective short-term, focused and easily implemented treatment for adults with NSSI. This 14-week long ERGT is administrated adjunctive to treatment as usual and aims at reducing NSSI for individuals with NSSI by directly targeting both NSSI and its proposed underlying mechanism - difficulties in emotion regulation. A newly conducted RCT on ERGT for adult women with BPD and self-injurious behaviors showed significant effects on NSSI and other self-destructive behaviors, BPD-symptoms, depression, anxiety, and emotion dysregulation [115]. These findings are consistent with previous studies evaluating ERGT [107,116].

2.3.4 MECHANISMS OF CHANGE IN THE TREATMENT OF NSSI

One of the most important research gaps within the field of psychotherapy research is to understand the mechanisms through which therapy leads to change [117,118]. Increased knowledge in this field has the potential of making already effective treatments even more effective. However, even for the most well-studied treatments, little is still known about the therapeutic mechanisms [119]. A first step to understand mechanism of change is through mediational analysis; that is, to study if a construct shows significant relationships between an intervention and outcome. To date, there are only a handful of studies investigating mediators in psychological treatments of NSSI [105,106,120-122]. Two papers have so far been published on potential mediators in ERGT, lending some support for the hypothesis that improvement in emotion regulation (as measured with the DERS) contributes to reduction in NSSI [120,121]. However, emotion regulation has to the best of my knowledge never been shown to mediate treatment outcome in adolescents.

2.4 ONLINE PSYCHOLOGICAL TREATMENT

Guided internet-based CBT (ICBT) has been shown to be effective for several mental disorders, such as depression and anxiety disorders in both adults (for a review, see Anderson [123]) and adolescents (for a review, see Vigerland et al. [124]). In guided ICBT, the therapy is based on online self-help material, supported and guided by a therapist communicating through the online platform [123]. A systematic review provides evidence that ICBT is at least as efficacious as traditional CBT for adults across a range of disorders [125]. One of the main advantages of ICBT compared to traditional CBT administered face-to-face is that it can increase the accessibility to evidence-based interventions [118]. Not only does ICBT carry the

potential to eliminate effects of geographical distance between therapist and patient and allow for less therapist time per patient. ICBT may also be perceived as convenient as patients do not have to schedule therapist appointments during their work or school day and can interact with the treatment manual when it suits them. Furthermore, there is research indicating that individuals with stigmatizing illnesses are more likely to use the internet than traditional health care to seek help [126]. Indeed, a recent study showed that one third of adolescents and young adults with a prior history of NSSI, reported that they had used the internet for help-seeking [127], suggesting that online treatment may be particularly useful in the treatment of NSSI. Although, there have been some recent efforts to treat suicidal thoughts and behaviors through the internet (e.g., [128,129]), online therapy has to the best of my knowledge never been studied specifically for NSSI.

2.5 SUMMARY

NSSI and NSSI disorder are common, particularly among adolescents, and have been associated with a variety of adverse outcomes, including various forms of psychopathology and suicide attempts. It has been recommended to study self-injury separately from suicidal behaviors to better understand its etiology and maintaining factors, thus informing assessment, clinical care and treatment development. Emotion regulation may be important in understanding NSSI, and the DERS is a useful measure of the construct. DBT and MBT have gained some support for their potential effects on NSSI, however the results are mixed and these treatments are not available to all. ERGT has shown promise in reducing adult NSSI and related difficulties among adult women. There is preliminary evidence that emotion regulation, as measured with the DERS, is a potential mechanism of change in ERGT. Several studies indicate that online interventions could increase the availability of effective treatments. However, online interventions have never been evaluated specifically for NSSI.

3 AIMS OF THE THESIS

The aim of the present thesis was to study clinical and psychosocial correlates and outcomes associated with NSSI, to develop a brief measure of emotion regulation, and to develop and evaluate novel treatments that can be easily and widely implemented for individuals who engage in NSSI.

The specific objectives and hypotheses for each study in this thesis were:

Study I: **Objective:** To compare the clinical and psychosocial correlates and subsequent adverse outcomes of youths with self-harm (SH), SH and suicidal ideation and behaviors (SH+SIB), and adolescents without any indication of SH or SIB.

Hypothesis: We expected that the presence of SH and SH+SIB would be associated with a higher problem load and subsequent adverse outcomes compared with clinical controls. Further, we expected adolescents who presented with SH+SIB to be more burdened and have poorer long-term outcome than patients with only SH.

Study II: **Objective:** To develop a brief version of the DERS (the DERS-16) and evaluate its psychometric properties.

Hypothesis: We expected that the DERS-16 would demonstrate high internal consistency and test-retest reliability. We also expected that the strength of the associations of the 36-item and 16-item versions of the DERS with measures of relevant constructs would be comparable.

Study III: **Objective:** To investigate the feasibility and utility of ERGT when administrated in Swedish psychiatric health care.

Hypothesis: We hypothesized to find significant improvements from pre-treatment to post-treatment in NSSI and other self-destructive behaviors, difficulties in emotion regulation, psychiatric symptoms, and adaptive functioning, as well as stability of these improvements during the 6-month follow-up period.

Study IV: **Objective:** To examine the feasibility, acceptance, utility of, and potential mechanism of change in, emotion regulation individual therapy (ERITA) when delivered face-to-face

Hypothesis: We expected that the credibility and acceptability of ERITA would be high and that we would find significant improvements from pre- to post-treatment in NSSI, other self-destructive behaviors, emotion regulation difficulties, and BPD symptoms, as well as stability of these improvements

during a 6-month follow up period. Finally, we also expected that change in emotion regulation difficulties would mediate improvements in NSSI during treatment.

Study V: **Objective:** To investigate the feasibility, acceptability, and utility of, and potential mechanism of change in, ERITA administered online.

Hypothesis: We expected high levels of treatment module completion and low treatment attrition and that the credibility and satisfaction of this treatment would be high. Further, we expected to find significant improvements from pre- to post-treatment in NSSI, emotion regulation difficulties, acceptance, global functioning, BPD symptoms, as well as parents' ability to respond effectively to their children's negative emotions. We also anticipated that these improvements would be maintained or further improved upon during 3- and 6-month follow up periods. Finally, we hypothesized that change in emotion dysregulation would mediate improvements in NSSI and self-destructive behaviors during treatment.

4 EMPIRICAL STUDIES

The studies included in this thesis cover a broad field of research including epidemiology, psychometrics, and intervention studies within the field of NSSI and emotion regulation. In this thesis, I have chosen to present the most recent study first, as it provides a good foundation for the following studies. Thus; first, I describe how we explored clinical and psychosocial correlates and subsequent adverse outcomes in adolescents presenting at child and adolescent mental health services (CAMHS) with SH and SH+SIB compared to clinical controls. Second, I depict the process of developing and evaluating a brief self-report measure that assesses difficulties in emotion regulation, a construct that may play an important role in the development, maintenance, and treatment of NSSI. Third, I outline how we evaluated ERGT in a multi-site feasibility trial for adult women with NSSI. Fourth, I describe the adaption of the ERGT-treatment for adolescents and the evaluation in an uncontrolled face-to-face pilot study. Finally, in an attempt to increase accessibility to psychological treatment for NSSI among adolescents, I outline how the adolescent treatment was adopted to an online format and studied in an uncontrolled pilot study.

The methods for these studies are thoroughly described in the respective papers. In this section, I will describe the methods and results for each study briefly and take the opportunity to complement some of these descriptions with additional information and results not mentioned in the papers.

4.1 STUDY I: CLINICAL AND PSYCHOSOCIAL CORRELATES AND SUBSEQUENT ADVERSE OUTCOMES OF SH AND SH+SIB

There is a need for large studies comparing correlates and outcomes between individuals with SH, SH+SIB, and clinical controls without SH or SIB. If it could be shown that these groups differ in terms of clinical correlates and adverse outcomes this would bring the field forward in terms of diagnostic and phenomenological clarity and should inform both risk assessment and treatment.

4.1.1 METHODS

We conducted a case-control study and a longitudinal cohort study using data from a regional clinical care register in Stockholm County Council that was linked to several Swedish national registers. The case-control study included all patients (5-17 years) within CAMHS between 2011 to 2015 (N = 25,161). Cases with SH and SH+SIB were compared with controls (patients without SH and SIB) regarding clinical care consumption (i.e., number of CAMHS visits, admissions to and number of nights in psychiatric inpatient care, and psychotropic medication), global functioning, mental disorders, and psychosocial problems. The longitudinal study included adult former CAMHS patients (N = 5,370) who were followed for a median time of 2.8 years after termination of CAMHS contact regarding the following outcomes: (1) any record of alcohol or substance use disorder; (2) recurrent care due to self-

injury; (3) psychiatric inpatient care; (4) dispensed psychotropic medication; (5) social welfare; (6) conviction/suspicion of a violent crime; and (7) conviction/suspicion of a non-violent crime.

4.1.2 RESULTS

In the case-control study, the SH group had more visits to CAMHS ($\beta = 7.3$, 95% CI [5.3–9.6]), lower global functioning ($\beta = -1.9$; 95% CI [-3.1--0.8]), and higher odds of having depressive (OR = 2.3; 95% CI [1.7–3.1]), anxiety (OR = 1.8; 95% CI [1.4–2.4]), and eating disorders (OR = 1.8; 95% CI [1.1–3.2]) compared to controls. In most comparisons, the SH+SIB group had more problems than the SH group. In the longitudinal study, the same pattern emerged for most outcomes; for example, the adjusted hazard ratio (HR) for recurrent care due to self-harm was 23.1 (95% CI [17.0–31.4]) in the SH+SIB group compared to HR = 3.9 (95% CI [2.3–6.7]) in the SH group. The corresponding HRs for inpatient care were 11.3 (95% CI [8.9–14.4]) vs. 1.7 (95% CI [1.0–2.7]), and for social welfare: 2.6 (95% CI [1.6–4.3]) vs. 1.5 (95% CI [0.8–2.7]).

4.1.3 CONCLUSIONS

Adolescents presenting to CAMHS with SH are more burdened in terms of clinical care, global functioning, mental disorders, and psychological problems, than clinical controls. Furthermore, this is a patient group with higher risk for several important adverse outcomes in emerging adulthood. The SH+SIB group were even more burdened and had even greater risks than the SH group in most comparisons. The results indicate a worse prognosis among CAMHS patients who present with SH and substantially worse among those with SH+SIB, which suggest that both SH and SIB need to inform risk-assessment and treatment.

4.2 STUDY II: DEVELOPMENT OF A BRIEF VERSION OF THE DERS (THE DERS-16) AND AN EVALUATION OF ITS PSYCHOMETRIC PROPERTIES

Findings from Study I highlight the importance of developing and evaluating early interventions for individuals with NSSI. In the process of evaluating interventions it is essential to also study potential mechanisms of change. As mentioned in the Introduction, there is preliminary evidence that emotion regulation (as measured with the DERS) mediates reductions of NSSI following treatment [120,121]. However, in the study of potential mechanisms of change it is important that both the mediator and the outcomes are assessed frequently with tight intervals during the treatment [130]. If a scale is to be administered often (e.g., weekly) it must be brief. A brief measure can also be used in clinics with limited time resources and large-scale epidemiological studies. Thus, a shortened version of the DERS would likely be an important contribution to clinicians and researchers.

4.2.1 METHODS

We developed a brief version of the DERS (the DERS-16) in collaboration with Dr Gratz (the author of the original DERS). The short-form was developed on the basis of both item-total correlations (on data obtained from the original study of the full-length version of the DERS [96]) and considerations regarding content validity. The psychometric properties of the DERS-16 were studied parallel to the ERGT study (Study III, see below) in a Swedish clinical sample ($N = 96$) and two US community samples ($Ns = 102$ and 482). The DERS-16 was administered twice for 31 participants to evaluate its test-retest reliability. The convergent and discriminant validity of the DERS-16 was examined comparing the strength of the association of the DERS-16 and the original DERS with measures of emotion regulation and related constructs, psychopathology, and clinically relevant behaviors theorized to stem from difficulties in emotion regulation.

4.2.2 RESULTS

Results demonstrated that the DERS-16 showed excellent internal consistency (Cronbachs' $\alpha = .92-.94$), good test-retest reliability ($\rho_t = 0.85$; $p < 0.001$), and good convergent and discriminant validity, and saves administration time compared to the 36-item version ($p < .001$). Further, the DERS-16 demonstrated small differences in its convergent and discriminant validity with relevant measures when compared to the original DERS.

4.2.2.1 Additional Results

The factor structure was not explored in the published paper on Study II because we suspected the study to lack adequate power for a confirmatory factor analysis (CFA) of the five sub-scales included in the DERS-16 (i.e., nonacceptance of negative emotions, inability to engage in goal-directed behaviors when distressed, difficulties controlling impulsive behaviors when distressed, limited access to emotion regulation strategies perceived as effective, and lack of emotion clarity). However, a CFA was conducted after this paper was published on the Swedish clinical sample ($N = 96$) using the lavaan R package for structural equation modeling [131]. In this CFA, a maximum-likelihood estimation with robust standard errors, suitable for data that are not normally distributed, was employed. The CFA demonstrated that the chi-square test of goodness-of-fit was significant, $\chi^2(94) = 136.98$ which indicates poor model fit. However, RMSEA = 0.069 (90% CI, 0.045, 0.090), SRMR = 0.085, and CFI = 0.954 suggests acceptable model fit [132].

4.2.3 CONCLUSIONS

The DERS-16 offers a valid and brief method for the assessment of overall emotion regulation difficulties. Post-hoc analyses provide preliminary evidence that the DERS-16 may also be used to assess the construct's different facets.

4.3 STUDY III: FEASIBILITY AND UTILITY OF A NOVEL TREATMENT FOCUSING ON EMOTION REGULATION –ERGT– WHEN ADMINISTRATED IN SWEDISH PSYCHIATRIC HEALTH CARE

Difficulties in emotion regulation was significantly correlated with NSSI in two out of three samples in Study II. One treatment that was designed to decrease NSSI in adults by targeting difficulties in emotion regulation is ERGT. However, ERGT had never been evaluated in traditional clinical settings and the extent to which ERGT could be disseminated to community clinicians was not clear.

4.3.1 METHODS

4.3.1.1 Adapting the ERGT-manual to a Swedish context

We translated the ERGT manual as well as the adherence and competence forms to Swedish in close collaboration with Drs Gratz and Tull (the authors of the ERGT manual). Examples and metaphors from the manual were culturally adapted, to better suite a Swedish context.

4.3.1.2 Therapist selection and training

An open invitation was addressed to potential participating therapists and clinics was distributed using different national networks. The therapists were required to have a regulated profession (e.g., a licensed nurse or psychologist) and have basic training in CBT (preferably with additional training in acceptance and commitment therapy and/or DBT). When we selected the participating clinics, we also considered the clinics geographical location (to assure geographical representation). We selected 15 clinics (out of 32 which had responded to the invitation), with two therapists per clinic. Thirty clinicians were thus provided with the ERGT-manual and relevant articles on NSSI and the theory underlying the treatment. The therapists were instructed to study this material before participating in a three-day ERGT workshop delivered by the originators of the treatment Drs. Gratz and Tull. During this workshop, the therapist not only learned how to deliver ERGT but we also provided detailed instruction on the study procedures. Before the study started, we also visited all clinics to ensure that the therapists understood the procedures and to identify potential local barriers to follow study procedures. The participating clinics were reimbursed for the administrative costs of the implementation.

4.3.1.3 Design

Ninety-five women (aged 18-49; $m = 25.1$; $sd = 7$) with threshold and subthreshold BPD and repeated NSSI were included in a multi-site trial, using an uncontrolled trial design with online assessments at pretreatment, post-treatment, and 6-month follow-up. The primary outcome was NSSI frequency. Secondary outcomes included NSSI versatility, difficulties in emotion regulation, other self-destructive behaviors, depression, anxiety, stress symptoms, and interpersonal and vocational difficulties. The study was conducted at 14 adult outpatient psychiatric clinics across Sweden. A total of 17 ERGT group treatments were conducted. All

sessions were filmed and reviewed to ensure therapists' treatment adherence and facilitate treatment supervision.

4.3.2 RESULTS

Ninety-three percent of the participants completed the post-treatment assessment and 88% completed the follow-up assessment. At post-treatment, analyses revealed a significant increase in past 4-month NSSI abstinence (17.9%; $p < .001$), moderate effect size on NSSI frequency (52% reduction, 95% CI [33, 66]; Cohen's $d = 0.52$, 95% CI [0.30, 0.75]), as well as significant improvements in NSSI versatility ($d = 0.41$, 95% CI [0.19, 0.63]), difficulties in emotion regulation ($d = 0.91$, 95% CI [0.63, 1.20]), other self-destructive behaviors (29% reduction, 95% CI [14, 41]; $d = 0.43$, 95% CI [0.20, 0.65]), and general psychiatric symptomatology ($ds = 0.30$ - 0.50). These results were either maintained or further improved at 6-month follow-up; for example, NSSI abstinence increased significantly (25.3%; $p = 0.01$) between post-treatment and follow-up.

4.3.3 CONCLUSIONS

ERGT seem to be a feasible, useful, and transportable treatment for NSSI and other self-destructive behaviors, difficulties in emotion regulation and psychiatric symptoms when delivered by clinicians in the community for adult women with subthreshold or threshold BPD.

4.4 STUDY IV: FEASIBILITY, ACCEPTANCE, AND UTILITY OF EMOTION REGULATION INDIVIDUAL THERAPY FOR ADOLESCENTS (ERITA)

As demonstrated in Study III, ERGT is a useful treatment for NSSI among adults. However, there is still a need for viable treatment options for adolescent with self-injurious behaviors. As previously described, the onset of NSSI is in early adolescence, and early interventions may potentially prevent later adverse outcomes. The principles of teaching emotion regulation skills for individuals with self-injury has proven to be effective in our and previous ERGT studies and we wanted to investigate if this treatment could be effective for adolescents. We began with conducting a pilot trial to investigate the potential feasibility and utility of ERITA, an individual treatment based on the ERGT protocol.

4.4.1 METHODS

4.4.1.1 Adapting the ERGT treatment to adolescents

Rationale for the individual treatment format. The adaptation of the treatment manual was conducted in close collaboration with Drs. Gratz and Tull. After careful consideration, it was decided that the adolescent version of ERGT would be delivered as an individual treatment as opposed to a group treatment. The main rationale for this was to improve safety for the participants. There is research indicating that frequency of self-injury may sometimes be influenced by social contagion (for a review, see Jarvi et al. [41]). Further, although

psychological interventions for adolescents that include group elements may be effective (e.g., MBT-A [106] and DBT-A [105]), some research indicates that group therapy for self-injurious behavior does not always lead to reductions in the behavior [133] and can even lead to increased self-injury frequency [134]. Although MBT-A and DBT-A show preliminary efficacy in reducing self-injurious behaviors, these treatments are combinations of group and individual therapy, allowing the risk for social contagion to be specifically addressed in the individual therapy. As this is not the case in ERGT, the ERGT-protocol was adapted from a group format to an individual format. Because ERGT is a structured treatment focusing on providing patients with skills (i.e., a skills group) rather than being an unstructured group where the group members talk about their difficulties and get support from one another (i.e., ERGT is not a process group), this was a fairly straightforward process, accomplished by adapting the group exercises to individual exercises. ERITA delivered in an individual setting offers a number of potential advantages over a group therapy approach. These may include: (a) no risk for the adolescents to reinforce NSSI amongst the other group members, (b) the treatment interventions can be tailored in a greater degree for the specific individual and his/her context, and (c) the treatment can be delivered in the respective participant's own pace.

Condensing the treatment. We also wanted the treatment to be shorter than ERGT in order to fit in one school semester. We therefore deleted one treatment session and combined four other sessions into two sessions (i.e., the session on primary vs. secondary emotions was combined with the session on clear vs. cloudy emotions, and the session on valued direction was combined with the session on commitment to valued actions). Further we added one final session on relapse prevention aiming to help the adolescent to identify which skills that had been most helpful, identifying risk situations, and strategies for preventing relapse. These changes resulted in a total of twelve sessions.

Impulsivity. As there is evidence indicating that impulsivity peaks during adolescence [135] we moved the impulse control session to a place earlier on in the treatment (session 2) to be able to provide skills for this in the beginning of the treatment. We also put more emphasize on other impulsive destructive behaviors (e.g., drinking, purging, and impulsive self-destructive sex) throughout the whole course of the treatment.

Youth-friendly design. The treatment was made more youth friendly by making the homework sheets simpler, including applying a youth-friendly design and format (incorporating colorful illustrations) and examples appropriate for adolescents.

Parent program. We included a parent program because parents are a significant part of the adolescents' daily life, and research indicates that family support is important in the treatment of adolescents with NSSI [136]. The parent program was developed as an online program with therapist support. This program consisted of seven online modules including information about NSSI and other risky behaviors, emotional awareness, effective

communication skills (e.g., validation [72]), and strategies to increase healthy activities (both together with the adolescent and for him- or herself), conflict management, and problem solving.

Safety precaution. In accordance with Swedish law, the therapists were legally obliged to share information about the adolescent's health condition on the caregivers' request (although, from the age of 15 the adolescent gain gradually increasing right to integrity by law). However, given that we as therapists needed to be able to fully rely on the adolescent's reports about their own well-being and the adolescent may feel a need to censor what they tell us if they do not want their parents to have access to certain parts of their life, therapists have to balance the need for parent involvement and what is best from a psychotherapeutic standpoint. This was achieved by making a pre-treatment agreement with the parent and the adolescent, including mutual understanding on how and under what circumstances information about the adolescent was to be shared with the parent. This usually meant that we made sure that the parents were fully aware of the methods, frequency and severity of their child's self-injurious behaviors and potential suicidal ideation at baseline. The agreement clearly stated that the parent would be informed only if the adolescent's mental health deteriorated and/or if new information had emerged. However, it was up to the adolescent to choose how their parent would receive the information, for example the adolescent could choose to (1) talk to the parent(s) him-/herself or (2) ask the therapist to do it together with him/her or (3) that the therapist informed the parents without the adolescent being present. Our aim was to provide the youth with maximum sense of control over how the communication took place, without having to compromise with regard to what information was shared.

Because NSSI is one of the strongest predictors for future suicide attempt [67-69], we needed to have a safety system around the patient and family. First, the participants were instructed to complete online weekly assessments of NSSI and suicidal ideation in order to detect sudden deterioration. Further, a crisis plan, involving concrete steps for the adolescents to take if they found themselves in a risk situation (e.g., increased suicidal ideation), was established before treatment start. This crisis plan was individualized for each adolescent who had agreed to each step in the crisis plan. The main function of the plan was to (1) make sure that the family had all the contact information required if the adolescent deteriorated and was in need of professional help (e.g., phone numbers) and (2) make a commitment together with the adolescent (and parent[s]) as to what they should do in case of emergency.

4.4.1.2 Study design

Seventeen girls (aged 13–17; $m = 15.3$; $sd = 1.4$) with NSSI disorder and their parents were included in an uncontrolled open pilot study. Self-report and clinician-rated instruments of the primary outcome NSSI and the secondary outcomes of other self-destructive behaviors, difficulties in emotion regulation, BPD features, and global functioning were administered at

pre-treatment, post-treatment, and 6- month follow-up. NSSI and difficulties in emotion regulation were also assessed weekly during treatment. All sessions were filmed to facilitate treatment supervision and ensure therapists' treatment adherence.

4.4.2 RESULTS

The rate of treatment completion (88%) and ratings of treatment credibility and expectancy were satisfactory, and both treatment attendance and ratings of therapeutic alliance were strong (see Table 2 for a summary of the results). Analyses revealed significant improvements in past-month NSSI abstinence ($p = 0.031$) and large effect sizes in past-month NSSI frequency (42% reduction, 95% CI [8, 64]; Cohen's $d = 1.14$, 95% CI [0.60, 1.95]), emotion regulation difficulties ($d = 0.81$, 95% CI [0.23, 1.50]), self-destructive behaviors (44% reduction, 95% CI: 5, 67, $d = 0.82$, 95% CI [0.23, 1.81]), and global functioning ($d = 1.08$, 95% CI [0.51, 1.62]), as well as a medium effect size in past-month NSSI versatility ($d = 0.50$, 95% CI [0.07, 0.78]), from pre- to post-treatment. Moreover, all of these results were either maintained or further improved upon at 6-month follow-up (see Table 2). Finally, the indirect effect of time in treatment on NSSI improvement through change in emotion regulation was significant ($ab = -0.02$, $SE = 0.01$, $p = .046$).

4.4.3 CONCLUSIONS

Results provide preliminary support of the acceptability, feasibility, and utility of ERITA for adolescents with NSSI disorder. Further, change in difficulties in emotion regulation mediated improvements in NSSI over the course of treatment.

4.5 STUDY V: FEASIBILITY, ACCEPTANCE, AND UTILITY OF ONLINE ERITA

One of the aims of this thesis was to develop a novel, targeted, and effective intervention that could be easily and widely implemented at a low cost. As an aforementioned review [122] shows, ICBT is effective for several psychiatric symptoms, including depression and anxiety disorders in adolescents. Moreover, ICBT carries several advantages compared to traditional face-to-face treatments that can increase accessibility to psychological treatment and may be particularly useful for individuals with stigmatizing illnesses given its association with shame [80] and low levels of disclosure [79]. Thus, following the development and pilot testing of ERITA face-to-face, we developed and evaluated an online version of this novel treatment.

4.5.1 METHODS

4.5.1.1 Development of the online ERITA

Several online psychological treatments for children and adolescents have been developed and evaluated [137-141] within the Child Internet Project (*Barninternetprojektet*; BIP) in Sweden since 2011. The BIP-platform was also used for the evaluation of online ERITA. This platform is entirely web-based, designed to be used by both adolescents and their parents and includes age-appropriate design, animations, and interactive scripts (see Figure 2). We made some modifications to the content in both the adolescent and parent treatment in response to therapist and participant feedback from the Study IV.

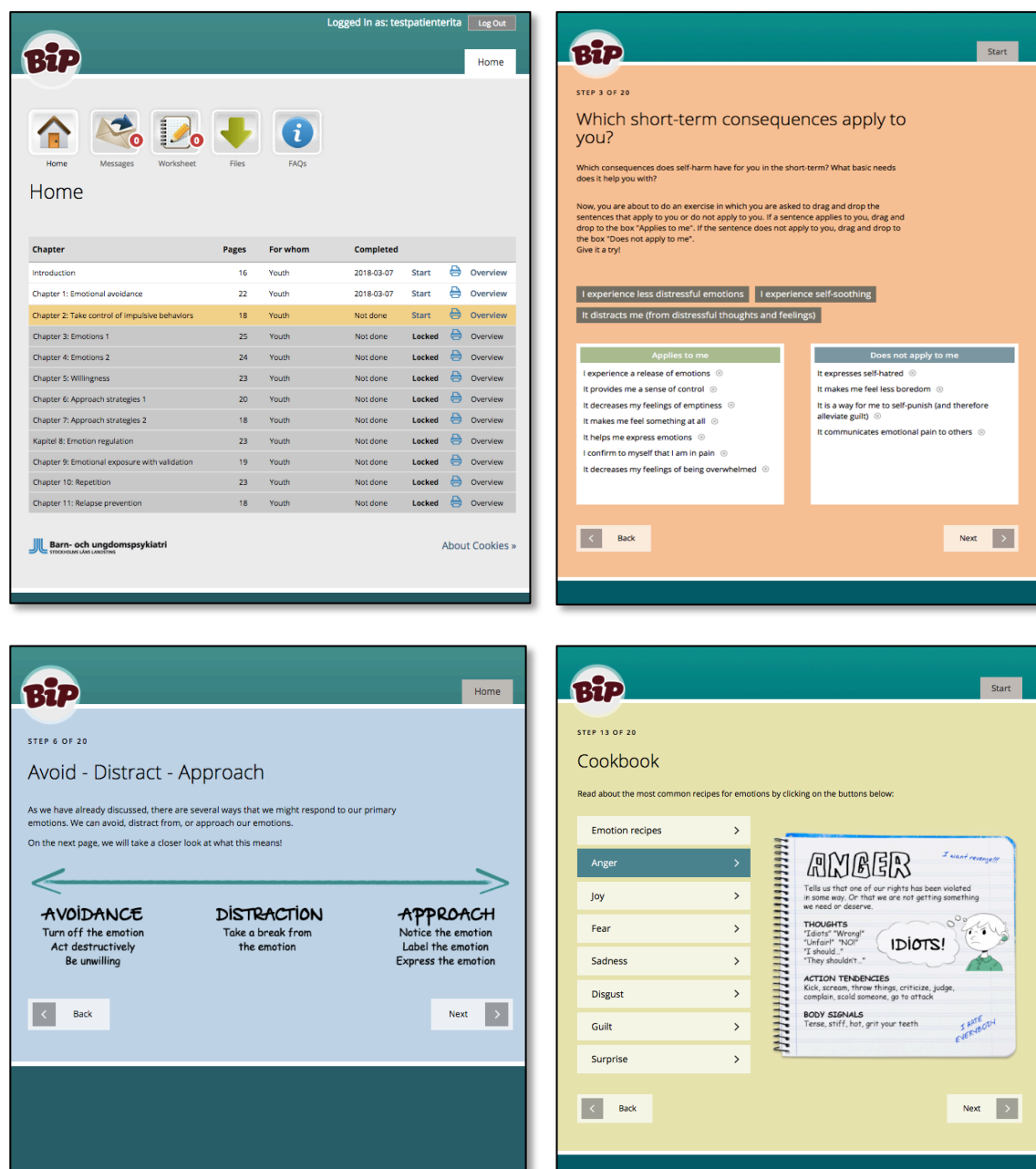


Figure 2. Screenshots of treatment module overview, interactive scripts, and psychoeducative animations and texts in online ERITA

Modifications to the adolescent treatment. The online ERITA included a greater emphasis on the practice of emotional approach strategies throughout the treatment, compared to face-to-face ERITA. As mentioned previously, there is a convincing body of research suggesting that NSSI is a negatively reinforced behavior (i.e., serves an avoidant function). Avoidance strategies are problematic, in part because they may prevent the extinction of conditioned emotions [142]. One way to address this could be repeated exposure to the stimuli that elicits the emotion while at the same time blocking the avoidance response [143], which has been suggested as an intervention for NSSI [71]. Explicit rationale for both imaginal and in-vivo exposure exercises was therefore included in the online treatment protocol of ERITA. Hence, the participants were instructed to identify and actively approach stimuli that elicit emotions that historically have triggered NSSI episodes for the individual (however, as discussed later in this thesis, some of these instructions have been removed in the online protocol that currently is being evaluated in a new trial). Further modifications in the online ERITA included moving information on valued directions and actions to the first module (vs. the end of treatment) to provide a rationale for approaching/exposing to emotions early in treatment. Finally, the four sessions on emotional acceptance, awareness, and clarity were combined into two modules, and the two sessions on emotional unwillingness and willingness were combined into one module.

Modifications to the parent program. In response to therapist and participant reports, we wanted to place greater emphasis on emotional awareness and validation in the parent program. This was done by replacing the conflict-management and problem-solving sessions with one module on the function and awareness of emotions and two modules on validation and invalidation. In addition to this, the parents got access to the adolescents' treatment, week by week (i.e., pdfs of psychoeducation and exercises, not answers provided by the adolescent) in order for the parents to be informed about the content of the treatment.

Therapist contact. During the course of the treatment (i.e., during 12 weeks) therapists (licensed psychologists) had regular online contact via the message functions in the BIP-platform with the participants in order to reinforce treatment engagement, problem-solve and answer questions when necessary, as well as assisting them in planning and reviewing homework assignments (see Figure 3). The assigned therapist was the same clinician that conducted the intake interview.

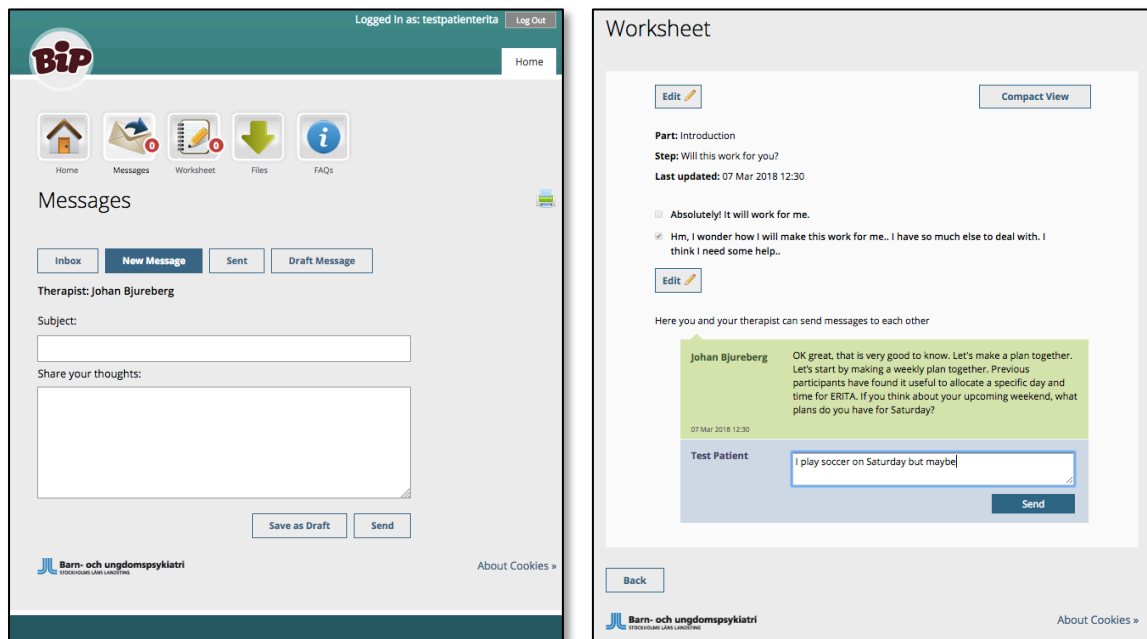


Figure 3. Screenshots of the message functions in online ERITA

The app. We developed a mobile app for this study as a complement to the online treatment. In the face-to-face ERITA, participants reported self-destructive behaviors and impulses to engage in these behaviors by completing daily pen and paper worksheets. However, inspired by ambulatory assessment [144], the app provided the participants with the opportunity to register self-destructive behaviors, impulses to act destructively, and on potential protective factors, on a daily basis. Furthermore, the mobile app (see Figure 4) included several built-in programs providing assistance in the skills acquired in the online treatment (e.g., impulse control strategies, emotional awareness and clarity, and distraction and approach strategies), and reminders of homework assignments. Further, the crisis plan could easily be accessed through the app.

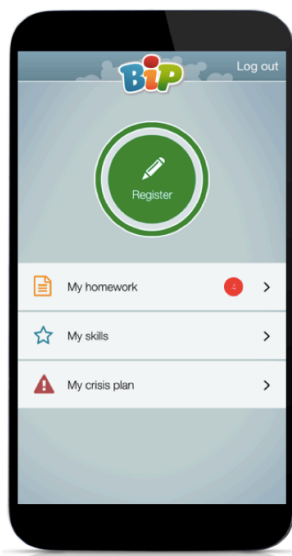


Figure 4. Screenshot of mobile app from online ERITA

Participant safety. As in Study IV, participant safety was ensured by pre-treatment agreements and weekly assessment of NSSI. In addition to this, the mobile app facilitated daily reports of NSSI as well as access to the individualized crisis plan, which may have provided additional safety.

4.5.1.2 Study design

Twenty-five adolescents (19 girls, 1 boy, 5 other [i.e., non-binary]) aged 13-17 ($m = 15.7$, $sd = 1.3$) with NSSI disorder and their parents were included in an uncontrolled open trial. The primary outcome measure was past-month NSSI and secondary outcomes included, NSSI versatility, self-destructive behaviors, difficulties in emotion regulation, and global functioning. These measures were assessed at pre-treatment, post-treatment, 3- and 6- month follow-up. Measures of NSSI, self-destructive behaviors and difficulties in emotion regulation were also assessed weekly during treatment.

4.5.2 RESULTS

Ratings of treatment credibility, expectancy, and satisfaction were acceptable, and the therapeutic alliance and treatment completion rate (96%) were high. No serious adverse events were reported. Adolescent participation in the treatment was associated with a statistically significant increase in past-month NSSI abstinence ($p = .007$), large improvements in past-month NSSI frequency (55% reduction, 95% CI [29, 72]; Cohen's $d = 0.88$, 95% CI [0.73, 1.06]) and global functioning ($d = 1.01$, 95% CI [0.77, 1.32]), and medium improvements in difficulties in emotion regulation ($d = 0.75$, 95% CI [0.59, 0.90]) and NSSI versatility ($d = 0.63$, 95% CI [0.54, 0.77]) from pre- to post-treatment. These improvements were further strengthened at 3-month follow-up and maintained at 6-month follow-up (see Table 2). The online therapist-guided parent program was associated with small to large ($ds = 0.47$ - 1.22) improvements in adaptive parent behaviors, and these results were maintained or further improved upon at 6-month follow-up. Further, the indirect relation of time in treatment to NSSI reduction through change in emotion regulation difficulties was significant ($ab = -0.019$; 95% CI [-0.045, -0.003]). Likewise, the indirect relation of time in treatment to reductions in self-destructive behaviors through change in emotion regulation difficulties was also significant ($ab = 0.011$; 95% CI: 0.025, 0.001).

4.5.3 CONCLUSIONS

These results suggest that online ERITA is potentially an acceptable, feasible, and promising low-intensity treatment for adolescents with NSSI disorder. Further, in line with the theoretical model underlying ERITA, change in difficulties in emotion regulation mediated changes in both NSSI frequency and self-destructive behaviors over the course of treatment.

4.6 SUMMARY OF THE RESULTS FOR THE FACE-TO-FACE AND ONLINE ERITA TRIALS

A summary of the results from Study IV and Study V are presented below to facilitate comparison between the results of the two different treatment formats.

4.6.1 FEASIBILITY

In face-to-face ERITA two (12%) participants dropped out of treatment after session 2, compared to one participant (4%) who dropped out after the second module in the online ERITA. The average number of sessions attended in face-to-face ERITA was 10.29 ($sd = 3.37$; median = 12) out of 12 sessions (86%) compared to the average completed treatment modules in online ERITA that was 9.7 ($sd = 2.1$; median = 11) out of 11 modules (88%). In face-to-face ERITA, all enrolled participants completed post-treatment assessments and 15 (88%) completed 6-month follow-up assessments. This could be compared to 24 (96%) and 21 (84%) participants in the online ERITA trial. Moreover, one face-to-face ERITA session was 60-minutes long (excluding preparations), while the mean therapist time per module for the adolescents in online ERITA was 22 minutes.

4.6.2 ACCEPTABILITY

In the face-to-face trial, mean ratings of treatment credibility ($m = 6.14$, $sd = 2.07$) and expectancy ($m = 56.43\%$, $sd = 22.74$) completed after the first session were satisfactory and comparable with mean ratings of treatment credibility ($m = 6.5$, $sd = 1.1$) and expectancy ($M = 55.6\%$, $sd = 21.4$) in the online ERITA.

Two different versions of the Working Alliance Inventory [145] were used in the two trials. These versions included different items and different number of items which complicates direct comparison. However, the mean score for perceived alliance divided by the number of items was 5.4 ($sd = 1.7$) in the face-to-face trial and 5.0 ($sd = 1.3$) in the online trial, which indicates high and comparable therapeutic alliance.

4.6.3 UTILITY

Table 2. A summary of adolescent treatment outcome variables in Study IV and Study V at pre-treatment, post-treatment, and 6-month follow-up

Measure	Pre-treatment	Post-treatment	6-month	Pre to post	Pre to 6-moth
Count outcome	Median	Median	Median	% change	% change
Study	(Q1;Q3)	(Q1;Q3)	(Q1;Q3)	[95% CI]	[95% CI]
DSHI-9-frequency					
Study IV F-to-F ^a	8 (4;13)	2.5 (0;4.3)	0 (0;3)	42 [8–64]	79 [60–89]
Study V Online ^b	9 (3;15)	2 (0;8)	1 (0;6)	55 [29–72]	69 [45–83]
	Proportion	Proportion	Proportion	p-value	p-value
DSHI-9-abstinence					
Study IV F-to-F	0%	29%	53%	.031	<.001
Study V Online	0%	28%	40%	.007	<.001
Continuous outcome	Mean (sd)	Mean (sd)	Mean (sd)	Cohen's d	Cohen's d
Study				[95% CI]	[95% CI]
DSHI-9-versatility					
Study IV F-to-F	2.1 (1.5)	1.4 (1.2)	0.8 (1.0)	0.50 [0.07,0.78]	0.89 [0.47,1.23]
Study V Online	2.2 (1.2)	1.4 (1.3)	0.9 (1.0)	0.63 [0.54,0.77]	1.11 [0.96,1.35]
DERS					
Study IV F-to-F	122.7 (17.2)	109.7 (25.2)	100.6 (17.9)	0.81 [0.23,1.50]	1.40 [0.87,2.03]
Study V Online	125.6 (20.1)	110.6 (27.2)	99.7 (26.8)	0.75 [0.59,0.90]	1.20 [0.95,1.44]
BPFSC					
Study IV F-to-F	70.4 (10.7)	66.9 (12.6)	63.4 (11.3)	0.33 [-0.03,1.11]	0.69 [0.18,1.19]
Study V Online	67.1 (12.9)	67.3 (13.9)	64.4 (12.2)	0.02 [0.02,0.03]	0.23 [0.19,0.27]
CGAS					
Study IV F-to-F	51.2 (4.9)	56.6 (8.0)	61.1 (11.2)	1.08 [0.51,1.62]	1.94 [1.03 3.12]
Study V Online	52.4 (7.1)	60.0 (9.8)	63.2 (10.6)	1.01 [0.77,1.32]	1.44 [1.09,1.88]

Note. ^aERITA administered face-to-face, ^bERITA administered online. Test statistics are based on generalized estimation equation models using either a negative binomial or normal distribution for count and continuous data, respectively. Confidence intervals for Cohen's *d* are based on 5000 bootstrap replications. Abbreviations: BPFSC = Borderline Personality Feature Scale for Children, CGAS = Children's Global Assessment Scale, DERS = Difficulties in Emotion Regulation Scale, DSHI-9-frequency = Deliberate Self-Harm Inventory – frequency past month, DSHI-9-abstinence = Deliberate Self-Harm Inventory – abstinence past month, DSHI-9-versatility = Deliberate Self-Harm Inventory – versatility past month.

4.7 ETHICAL CONSIDERATIONS

In research, one has to weigh the importance and potential benefits of the research against the risks and burdens to the study participants. All studies in this thesis have been scrutinized and approved by appropriate research ethics committees. This thesis includes both intervention studies and register-based studies that pose different ethical challenges.

In Study I, several registers containing sensitive personal information that could harm the personal integrity of the study participants were used. Therefore, the identity of the participants was protected by the use of a unique identification code, and the researchers did not have access to any information that could link the code with a specific individual.

Participation in this study did not entail any immediate benefit for the participant. However, research using these types of registers can lead to increased knowledge that can inform assessment and treatment for others.

Study II-V include participation in more or less experimental and untested interventions. NSSI is associated with a variety of psychiatric issues, confers risk of physical injury, and is a risk factor for attempted suicide, presenting researchers and clinicians with a variety of ethical challenges that warrant consideration when conducting treatment studies. First, assuring that the participants are voluntary agreeing to participate in the research, the study therapists in Study II-V, informed the participants (and when appropriate the legal guardians) what they could expect if they chose to participate in the research and of their right to discontinue treatment. This information was provided in both verbal and written form and contact information was given in case of questions or uncertainties. Second, in order to ensure patient safety, all therapists received extensive briefing and training in the study protocol and safety routines. In addition, regular contact was established between the outpatient clinics, its directors and the research group throughout the study, in order to ensure patient safety and research integrity. Third, in Study III and IV, all sessions were filmed and reviewed weekly by experts in the treatment. This ensured adherence and competence and enabled detailed supervision each week. However, filming sessions raises concerns of patient integrity. Thus, this procedure was described in both the verbal and written information provided to participants. Special care was given to the security involved in uploading, reviewing, and storing of the filmed sessions. Fourth, because the participants included in studies III-V engaged in high-risk behaviors and may have an increased risk for sudden deterioration in mental health and may be in need of acute treatment not offered in these treatment studies, all patient contact was delivered within regular psychiatric clinics. This enabled us to use, and participants to benefit from, services within the regular care system, such as documentation, follow-up inside the health care, and possibility to refer the participants. Fifth, if participants were not included in the study or if included participants had not benefited from the treatment as intended, the research group facilitated further contact with regular mental health care. Sixth, in all intervention studies, screening and assessment of severity of NSSI and suicidal ideation was thorough and included weekly assessments of suicidality and frequency and severity of NSSI and other potential harmful behaviors. However, this implied an extra burden for the participants, and might have been perceived as demanding. To address this issue, we put large effort in selecting well-known, short and validated assessment tools in order to reduce this burden while at the same time maximizing patient safety and quality of data. Seventh, in Study V the treatment was delivered through the Internet. This raised unique ethical challenges as face-to-face interactions were limited during the study. However, the possibility of daily online contact provided the participant and therapist to communicate and detect sudden deterioration in mental health that is not possible in usual health care where the patient usually meets with his/her therapist only once or twice a week and does not have contact in between sessions. Further, the families had easy access to a crisis plan and if

necessary, telephone contact and/or personal visits could be arranged. Thus, in comparison to treatment as usual, the intensive surveillance of the patients in Study V could even lead to increased patient safety. Finally, all intervention studies included in this thesis were registered in the ClinicalTrials.gov trial registry.

In summary, balancing the need for studying correlates, outcomes, and treatments for individuals with self-injurious behavior with the individual need for integrity and safety has enabled the research group to include individuals who seldom seek treatment, and who would not otherwise have been offered participation in a treatment study. This could potentially lead to large benefits for the affected individual, their families, and society at large.

5 DISCUSSION

5.1 MAIN FINDINGS

SH with and without SIB before the age of 18 is associated with clinical and psychosocial burden and constitutes a risk factor for several adverse outcomes. Patients with SH+SIB are at greater risk than patients with SH only (Study I). ERGT, when implemented in regular health care delivered by clinicians in the community appears to be a feasible, transportable, and useful treatment for NSSI and related problems among adult women (Study III). The adapted version of ERGT for adolescents, ERITA, shows feasibility, acceptability, and utility in the treatment of NSSI among adolescents with NSSI disorder (Study IV). Online ERITA is also an acceptable, feasible, and promising low-intensity treatment for adolescents with NSSI disorder (Study V). The DERS-16 is a brief and valid measure that can be used for repetitive assessment of difficulties in emotion regulation (Study II). The DERS-16 was successfully used in the ERITA trials, showing that difficulties in emotion regulation mediated week-to-week improvements in NSSI (Study IV and V), and risk behaviors (Study V).

5.2 CORRELATES AND ADVERSE OUTCOMES

Results from Study I confirmed our hypothesis that CAMHS patients with SH had more clinical care, lower global functioning, presented with more mental disorders, and psychosocial problems than clinical controls. Patients with SH+SIB had even more problems in most areas. The findings from the longitudinal study were similar, in which SH was a risk factor for several negative outcomes and SH+SIB was associated with even higher risks. The results suggest that if an adolescent present to the CAMHS with SH or SH+SIB, clinicians need to assess and address the adolescent's present situation (in terms of global functioning, pharmacological treatment, comorbidity, and psychosocial burden). Study I also confirm that not only does the present situation need attention, but SH and SH+SIB are associated with elevated risks for several adverse outcomes in young adulthood.

The findings that SH and SH+SIB are associated with elevated risks may not come as a surprise to the reader, as problems are often associated with other problems. However, among

health care professionals, individuals with self-injurious behavior have been described as manipulative and attention-seeking [146], and there are even findings showing examples of clinicians perceiving individuals presenting with self-injury as time wasters and unworthy of treatment [147]. Indeed, a systematic review on caregiver's attitudes regarding individuals that harm themselves, confirm that both medical and psychiatric staff generally have a more negative attitude towards this group of patients compared to other patients [74]. This negative attitude is mirrored by experiences of Swedish health care service users with self-injurious behaviors [148], and the Swedish Agency for Health Technology Assessment and Assessment of Social Services concluded that these experiences discourage individuals with NSSI from future health care seeking [81]. These findings are consistent with a study showing that the majority of adolescents with self-injurious behavior never seek professional help [77]. My own personal experiences from project leading and recruiting participants to the clinical trials included in this thesis are that many health care professionals are devoted to deliver high quality support and professional treatment. However, I have also come across several examples of health care professionals that explicitly state that they do not believe that NSSI is in itself a reason for specialized psychiatric care, and that self-injurious behavior should be ignored and will cease by itself. However, in contrary to this belief, findings from Study I stress the importance that individuals with SH and SH+SIB should be a prioritized patient group within CAMHS.

5.3 THE NEED FOR EARLY INTERVENTIONS

So far, no treatment has consistently been shown to be superior than treatment as usual for NSSI [99,100]. Identifying subgroups of individuals with self-injury (e.g., differentiate between those who harm themselves with suicidal intent from those without suicidal intent) may have relevance for treatment development and treatment planning [98,136,149]. Health care interventions are often delivered step-wise, i.e., brief interventions are followed by more intense treatments, should improvement fail to appear. For those with higher risk and worse prognosis (i.e., those that present at CAMHS with SH or SH+SIB), more specialized treatment programs from start should probably be the preferred choice, rather than applying a "qualification approach" where access to more advanced or intense treatment is dependent on the progression of symptoms and behaviors. For example, based on a literature review of intervention studies, Brent et al. [136] recommend initializing treatment during inpatient care following an acute self-injurious event. Even though Swedish youth with SH and/or SIB commonly are provided specialist level care, more specialized treatments such as DBT or MBT rarely are available to those under 18 years of age [150]. Moreover, because these treatments are long, intensive, and expensive, it would not be possible to offer these treatments to everyone that engages in self-injurious behaviors [151]. A consequence of the lack of specific treatment programs for younger adolescents is that substantial time may pass between the onset of severe risk behaviors and enrollment in evidence-based interventions. Hence, effective early evidence-based treatments for individuals with self-injurious and

suicidal behaviors are urgently needed. One suggestion to address this need has been to develop adjunctive treatments that may augment the standard therapy provided by clinicians in the community [114]. Thus, the treatments that were developed and evaluated in this thesis were designed to be short, easily implemented, effective, and possible to deliver adjunctive to treatment as usual.

5.4 FEASIBILITY AND UTILITY OF ERGT IN PSYCHIATRIC HEALTH CARE

In Study II we implemented ERGT at 14 outpatient clinics delivered by 28 therapists. In line with our hypothesis, patient participation was associated with significant improvements from pre- to post-treatment in NSSI, other self-destructive behaviors, difficulties in emotion regulation, and symptoms of depression and stress. These results were maintained or further improved at 6-month follow-up. The results found from this study are similar to those obtained in previous ERGT efficacy trials [107,115]. Needless to say, they must be interpreted with caution because of the lack of a control group. However, one strength in this study was that the therapists had different professions (e.g., nurses, social workers, and psychologists) and are thus representative of the therapists who treat this patient population in the community. Hence, Study II provides unique data on how the treatment may actually perform when provided in routine clinical care under real-world conditions, thus providing preliminary support for the generalizability and transportability of ERGT. This type of study may play an important role in increasing the availability of an evidence-based treatment for NSSI. Indeed, before Study II was conducted, few professionals within Swedish psychiatric health care had any previous experience of ERGT. Since this study was conducted, we have organized several workshops (held by Drs. Gratz and Tull) and trained more than 120 therapists and 12 supervisors in ERGT throughout Sweden. The reasons behind this rapid dissemination of ERGT in Sweden is probably due to its promising effects [107,115,116] and funding from the National Self-Injury Project, but also due to its relative brevity compared to alternatives (e.g., DBT and MBT). Although shorter interventions that specifically target NSSI are much-needed, politicians that advocate shorter treatment alternatives must always be mindful of the research base of the treatment studies at hand. In my opinion, ERGT is a welcomed complement to treatment as usual but independent RCTs, including health care economic evaluations, are urgently needed before this novel treatment can substitute well-known alternatives. With that said, we have continued to collect data for some ERGT-groups after study termination, and it will be interesting to follow the ongoing dissemination of ERGT within Swedish health care.

5.5 FEASIBILITY, ACCEPTANCE, AND UTILITY OF FACE-TO-FACE ERITA

In line with the objectives and hypotheses, Study IV provides preliminary support for the feasibility, acceptability, and utility of ERITA in the treatment of NSSI and related difficulties among adolescents with NSSI disorder. Further, consistent with our hypothesis, change in difficulties in emotion regulation mediated improvements in NSSI over the course of

treatment. These findings add to the literature as the first attempt to study an adapted version of ERGT for adolescents, being one of the few treatments specifically developed to address NSSI in youth [152-154], and for studying mediation in treatment of adolescent NSSI. However, the absence of a control group precludes any conclusions regarding the effects of this treatment versus the passage of time or other factors.

5.6 FEASIBILITY, ACCEPTANCE, AND UTILITY OF ONLINE ERITA

Study V revealed findings consistent with those obtained in the face-to-face trial, with high ratings of treatment credibility and expectancy, therapeutic alliance, and treatment satisfaction indicating acceptability. Furthermore, only one participant dropped out of treatment, the majority of the participants completed all treatment modules, and no serious adverse events were reported, indicating feasibility. Moreover, statistically significant decreases in adolescent NSSI and difficulties in emotion regulation and increase in adaptive parental behavior suggest utility of online ERITA. These findings were consistent with qualitative analyses based on interviews with the adolescent and parent participants in the study, conducted as part of a master's thesis [155], suggesting that the flexibility inherent in online format (i.e., when and where the participant could engage in the treatment) and support (i.e., online contact with the therapist) were important contributing factors to a positive treatment experience. These findings are encouraging given that improving treatment compliance for adolescents engaging in NSSI is a critical first step in delivering effective treatments [99]. Importantly, however, the mean therapist time per adolescent in Study V was approximately one third of the time required in face-to-face ERITA or other brief treatments for NSSI (e.g., [152]). This reduction in therapist time was accomplished without any apparent loss in the feasibility, acceptance, or utility of the intervention. Thus, online ERITA has the potential to offer a specific, brief, and acceptable intervention that could easily be implemented in areas without viable treatment options and for adolescents who would not engage in treatment otherwise. Needless to say, the findings must be interpreted with caution because the absence of a control group limits any conclusions regarding causality.

5.7 MEANINGFUL CHANGE IN THE TREATMENT OF NSSI

There has been extensive critique against *p*-values, as it says little about practical importance, any particular alpha-threshold is arbitrary, and that the “difference between ‘significant’ and ‘not significant’ is not itself statistically significant” [156, p. 328]. To address this issue, many major journals advocate the use of reporting effect sizes. However, even with large Cohens’ *ds* or hazard ratios, it depends on the outcome of interest if the change or risk are of practical importance. However, one effect size that without doubt is meaningful is the proportion of participants that cease harming themselves in response to treatment. In the adult ERGT-trial, the proportion of participants that reported NSSI abstinence (i.e., zero NSSI episodes) the past 4 months increased significantly from 4.2% at pre-treatment to 17.9% at post-treatment

and to 25.3% at 6-month follow-up. This was lower than in previous ERGT trials [115,116] which may, as discussed in the paper, be attributed to differences in the level of therapist training provided in the study compared to previous trials or to differences in sample composition and/or symptom levels. In the adolescent trials about half of the participants reported NSSI abstinence at the 6-month follow-up. Few treatment studies on adolescent NSSI report this outcome, however in an evaluation of MBT-A, 44% reported self-injury abstinence after 12 months of intervention [106]. This comparison is promising for our short, low-intensive therapies for adolescents.

5.8 BEHAVIOR SUBSTITUTION

As previously discussed, NSSI decreases for many adolescents during the transition to adulthood [63,157]. When studying the behavior over time, it has therefore been recommended to follow up a broad range of risky behaviors [63], to answer the question if NSSI is substituted by other behaviors, such as alcohol or drug use. Tendencies of “symptom shifting” has been found in one study on developmental trajectories of NSSI, suicidal behavior and substance misuse [64]. Indeed, in Study I, the risk for alcohol misuse was more than doubled in the SH group compared to controls, which may indicate that some individuals either acquired an additional risky behavior or substituted self-injury with alcohol misuse (though this was never investigated). To control for behavior substitution in our intervention studies, we included a measure of risky self-destructive behaviors (the 11-item behavior supplement to the Borderline Symptom List [158]). In these studies, the observed decrease in NSSI was accompanied by a decrease in this measure, suggesting that the participants had not just replaced NSSI with other risky behaviors. Indeed, as Study V implies, increased skills in emotion regulation did not only mediate the decrease in NSSI, but also mediated week-to-week decrease in risky behaviors. The preliminary finding that the adolescents improve their skills in emotion regulation following ERITA is promising, especially considering the increased risks of adverse outcomes (some of which potentially could be due to difficulties in emotion regulation) observed in Study I, that these adolescents are at risk for in emerging adulthood.

5.9 MEDIATION

ERGT and ERITA were developed to reduce NSSI by teaching the participants more adaptive ways of responding to their emotions. The two studies on ERITA provide preliminary support for emotion regulation as a potential mechanism of change in this treatment of adolescent NSSI, as well as the theoretical model underlying the treatment. These findings also highlight the clinical utility of targeting emotion regulation in the treatment of NSSI and other self-destructive behaviors among adolescents. The mediation analyses were possible to conduct given that we assessed both the mediator and outcomes weekly during treatment. This is, to my knowledge, the first treatment studies for NSSI that follow recommendations for mediation [130] by assessing both the potential mediator and outcome with tight

intervals. However, although ERGT/ERITA are considerably more specific than many other prevailing treatment models for NSSI, they do include a multitude of emotion regulation skills. In order to better understand the role of emotion regulation in the maintenance of NSSI, future studies could benefit from dismantling designs isolating particular emotion regulation skills (such as emotional awareness or impulse control) by design and test its isolated effect on NSSI. An important approach in early treatment development phase is to use multiple baseline single-case designs [159]. These types of designs facilitate higher experimental control compared to open uncontrolled trials and can still be adopted on small sample sizes. These designs coupled with the comparison of short and distinct treatment modules may facilitate knowledge on the maintaining factors behind NSSI (see Bentley et al. [153] for an interesting example).

5.10 EXPOSURE

Explicit rationale for structured imaginal and in-vivo exposure exercises [143] were included in the online ERITA protocol. Hence, the participants were instructed to identify and actively approach stimuli that elicit emotions that usually triggered NSSI-episodes for them. However, during treatment it was evident that it was difficult for the participants to identify defined situations for such exposure. This was also verified in the qualitative interviews conducted with the participants [155]. In the treatment of other anxiety disorders, such as social anxiety disorder or obsessive-compulsive disorder it is often evident which stimuli (e.g., giving a speech or leaving the front door) that trigger the conditioned response. However, for individuals with NSSI, these situations may vary to a greater degree. For example, research has demonstrated a strong link between social rejection and NSSI [160] which often is a situation that triggers unwanted emotions that some individual avoids by harming themselves. However, the effect of social rejection may vary greatly within one individual in different contexts making it difficult to actively identify a situation for exposure. Therefore, the explicit rationale for exposure with response prevention has been removed in the revision of the online treatment currently being evaluated in a RCT. Instead, a greater emphasis is now once again on approaching aversive situations or emotions when they arrive and to flexibly try new strategies instead of avoiding (key interventions in ERGT and ERITA). Within this framework, behavioral exposure may focus on increasing alternative responses to the stimuli, such as approaching or staying in aversive situations or emotions and to flexibly try new strategies instead of avoiding [71].

5.11 HOW IMPORTANT IS THE PERSONAL THERAPIST CONTACT?

Being a study therapist and supervisor in Study IV and V provided me with clinical experience of the same patient group and the same interventions, but with different ways of delivering the treatment. I see apparent advantages with the online format. In addition to the advantages often mentioned (e.g., accessibility, less therapist time per patient, geographical distances, no need to schedule appointments, and less impact of therapist drift [i.e., clinicians'

failure to adhere to treatment protocol]), it may actually be an advantage that the personal contact is limited in online treatment. When watching video records of my own and others' sessions it is sometimes apparent that the patient is not mindful during the session, without the therapist really noticing this. Sometimes my impression is that the patient is so occupied with how he/she/ze is being perceived or with something that happened before the session, that it competes with being attentive on learning new skills. Indeed, there is psychotherapy research indicating that patients do not remember most of the session content after the session [161]. Further, although strong therapeutic alliance may be helpful, the therapist contact (e.g., in the case of bad personal matching between therapist and patient) may also interfere with therapy, especially for individuals (patients and therapists) with interpersonal difficulties. Finally, therapist drift (that is, clinicians' failure to deliver evidence-based therapy) is a common and well-studied barrier for effective treatments [162]. In online therapy, the patient can always revisit the session content and may choose to interact with the treatment material once he/she/ze is in the right state of mind, and the personal contact is limited to online communication.

It could very well be the case that online contact is less effective than face-to-face contact with effective therapists but may at the same time buffer for the potential detrimental effects of contact with ineffective therapists. Interestingly, the adolescents rated the therapeutic alliance very similar in Study IV and V, indicative that it may be possible to achieve strong therapeutic alliance through online contact with adolescents. Worth mentioning though, is that in both adolescent trials, the therapists also conducted the initial assessments which may have laid the foundation for strong therapeutic alliance. However, in the qualitative analyses of the online ERITA, participants reported that they felt supported by the online therapist and that it felt safe to share personal thoughts and feelings and attributed that to the online format [155]. In summary, repeated face-to-face contact may not be necessary in the treatment of NSSI among adolescents due to the structured treatment format, access to the treatment material, and the method of communication inherent to online treatment. However, if it would be possible to completely omit personal contact is another question (see Andersson [123]).

5.12 PSYCHOMETRIC PROPERTIES OF THE DERS-16

In order to be able to assess difficulties in emotion regulation weekly we developed a short version of the DERS, the DERS-16. In Study II, the brief version of the DERS demonstrated reliability and validity as a global measure of difficulties in emotion regulation. One limitation addressed in the paper of this study was that we did not explore the factor structure. The main reason was that we suspected the sample size to be insufficient to confirm the five-factor structure in a CFA. However, post hoc analyses included in this thesis provide preliminary evidence for the proposed factor structure in the DERS-16. Although these findings need to be interpreted with caution because of inconsistent model fit indices and low power, they are in line with recent studies that have provided independent evidence for the proposed 5-factor structure in the DERS-16 [163,164]. Thus, although this short version was developed as a

viable option in the assessment of overall emotion dysregulation, the additional analyses included in this thesis suggest that the DERS-16 may also be used to study the five different facets of the construct.

5.13 LIMITATIONS

The studies included in this thesis have some important limitations inherent to their design. These include that the registry study was based on administrative data and the treatment studies employed uncontrolled designs. Most importantly in Study I, the operationalization of cases/controls and exposed/unexposed were based on clinicians' judgement, and we know little about when and how SH and SIB were assessed. In studies III-V, the most important limitation was that the uncontrolled open trial design precluded any conclusions regarding causal inferences of potential treatment effects. Without control group we do not know if other factors may have, at least in part, accounted for the studies' findings, such as passage of time or factors underlying both treatment completion status and symptom improvement (e.g., motivation or therapeutic alliance). However, although the uncontrolled designs limit the ability to draw conclusions regarding treatment effect they can provide essential information on acceptability, feasibility, and potential adverse events associated with the treatment and procedure that may inform future RCTs. Recently, one of the largest (N = 832) and most expensive treatment studies ever conducted in the field of adolescent self-injury failed to provide evidence that a family therapy intervention was beneficial compared to treatment as usual [122]. A critique to that trial has been that an untested intervention should be explored stepwise [151] in pilot studies before beginning extensive trials.

Further, the usage of vague and inconsistent terminology for self-injurious behaviors has been proposed to be one of the greatest obstacles in the studies of the behavior [149], as different definitions may include different phenomena. Although we initially had an ambition to be consistent in the nomenclature, we have used several different terms for self-injurious behavior (i.e., SH, NSSI, and DSH) in the included papers in this thesis. The terms NSSI and DSH used in studies II-V has been defined as direct and deliberate destruction of body tissue without suicidal intent [165]. However, neither of these terms could be applied in Study I. In this study, the raters could choose between "self-injurious behavior" and "suicidal ideation and behaviors" as two separate predefined categories. Thus, we had to infer that if a clinician only documented SH (i.e., not suicidal ideation and behaviors) this would equal NSSI or DSH. However, because we did not know if the clinicians completed thorough assessment regarding suicidal intent we refrained from using those terms. During the past few years many scientists and clinicians have begun to use more clear and consistent definitions of these behaviors [149], which hopefully will improve our understanding of clinical registers in the future.

5.14 FUTURE DIRECTIONS

It is evident that self-injury is a serious behavior that needs to be addressed. However, its relationship to suicidal behavior needs further exploration. One way to study if there is a qualitative difference between nonsuicidal and suicidal behavior may be to study potential cross-over between the two behaviors over time, preferably in large registries with little missing data. This may inform: (a) if NSSI and suicidal behaviors should be considered as separate diagnostic entities, (b) why no single intervention has shown to be superior to treatment as usual for NSSI among adolescents when considered separate from suicidal behavior [99], and (c) if interventions aiming to reduce NSSI should differ from those aiming to reduce suicide attempts. Further research that would improve our understanding of maintaining factors of NSSI and how to best intervene may be to expand the research on self-reported reasons of harming one-self (i.e., to avoid aversive emotional states) by studying the biological mechanisms through which this occurs (e.g., endorphin release or distraction). As mentioned previously, the evidence base for interventions targeting NSSI is weak [99,100]. The novel treatments studied in this thesis all show potential; however, RCTs are needed to provide more rigorous data that can speak more broadly of the acceptance, feasibility, and efficacy of these treatments. One recent extension of this work is our ongoing RCT comparing online ERITA with treatment as usual in a national multi-center study. This study does not only carry the potential to speak to the potential efficacy of the treatment, but also addresses questions that can be answered by using momentary assessment, mediation analyses (including competing mediators), and health economy assessments.

6 CONCLUSIONS

Taken together, SH and SH+SIB should inform risk assessment and be prioritized within CAMHS. The DERS-16 is a reliable, valid, and brief self-report measure of difficulties in emotion regulation with broad clinical and research utility. ERGT is a treatment that can be easily implemented within health care and carries the potential to increase access to evidence-based treatments for NSSI. ERITA may be a promising treatment for NSSI among adolescents, both in a traditional face-to-face format as well as in an online format and should be evaluated in randomized controlled trials. Also, difficulties in emotion regulation as measured with the DERS-16 mediates week-to-week changes in NSSI during adolescent treatment, thus providing further preliminary support for the underlying role of emotion regulation difficulties in the maintenance of self-destructive behaviors, as well as for emotion regulation as a potential mechanism of change in ERGT-based treatments.

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